## REMARKS

***Status of the claims***

Claims 1-30 are pending in the present application and are currently under consideration. By virtue of this response, claim 1 has been amended. Support for the amendment to claim 1 may be found, for example, in paragraphs [0053], [0054], [0082], and [0110] of the specification. Accordingly, no new matter has been added by the foregoing amendment.

With respect to any claim amendments or cancellations, Applicants have not dedicated to the public or abandoned any unclaimed subject matter and moreover have not acquiesced to any rejections and/or objections made by the Patent Office. Applicants expressly reserve the right to pursue prosecution of any presently excluded subject matter or claim embodiments in one or more future continuation and/or divisional application(s).

***Telephone interview***

Applicants thank Examiner Cheu for the extending the courtesy of a telephone interview on March 4, 2005, and for the helpful discussion that ensued. Applicants have given careful consideration to the issues raised in the outstanding Office Action and in the telephone interview and believe that the Examiner's concerns have been addressed as described herein, thereby placing this case into condition for allowance.

***Supplemental Information Disclosure Statement***

Applicants are filing a Supplemental Information Disclosure Statement concurrently with this response. Applicants would appreciate the Examiner initialing and returning the Form 1449, indicating that the reference listed therein has been considered and made of record in this application.

***Rejection under 35 U.S.C. §102(b)***

Claims 1, 9-11, 12, 14, 16-26 and 28 stand rejected under 35 U.S.C. §102(b) as allegedly anticipated by Belov et al. (2001) *Cancer Res* 61:4483. Applicants respectfully traverse this rejection for reasons of record in the response filed on September 28, 2004, and for reasons discussed hereinbelow.

As discussed in the recent telephone interview, Belov et al. do not teach a set of digital antibodies that each bind a different epitope consisting of 3 or 4 consecutive amino acids, wherein each antibody in the set recognizes a plurality of proteins comprising the epitope to which the antibody binds, as currently claimed. The claimed digital antibodies recognize very small epitopes of 3 or 4 amino acids and are therefore each capable of binding to multiple proteins that comprise the epitope recognized by a particular digital antibody. Binding of a combination of digital antibodies to the proteins in a sample provides information such as, for example, presence or identity of one or more particular proteins of interest in a sample. The combination of digital antibodies provides a signature pattern of binding to a protein of interest. Information about a protein in a sample may be provided by comparison of an observed pattern of binding of multiple digital antibodies to the protein with a characteristic pattern of binding of the antibodies to a protein of interest. In contrast, conventional immunodetection methods, such as those taught by Belov et al., rely on detection of binding of a single antibody that is highly specific for a single antigen. As discussed in paragraph [0053] of the specification, the claimed antibodies "are useful *in combination* to generate a characteristic pattern of binding between antibodies in a set and protein in a sample, wherein the protein binding pattern, termed a protein binding profile, may be used to characterize, or "fingerprint" the protein sample. . . .*Thus, specificity of results and information arising from antibody binding is conferred via the binding of sets of digital antibodies to protein in a sample (whereby a specific protein binding profile is generated), rather than by binding of a single antibody that binds but one or a few proteins, as commonly used in the art for specific detection.*" (emphasis added)

The Examiner states that it is an inherent characteristic that recognizable epitopes for antibodies usually consist of 3, 4, or more consecutive amino acids. Office Action, page 3.

Applicants respectfully disagree with the statement that the claimed digital antibodies are inherently disclosed in Belov et al. As an initial matter, Applicants respectfully note that none of the claims recites an epitope consisting of "3, 4, *or more* consecutive amino acids," as set forth by the Examiner on page 3 of the Office Action (emphasis added). The claims recite a set of digital antibodies comprising at least 15 digital antibodies that each bind an epitope *consisting of 3 or 4 amino acids*. There is no recitation of the phrase "or more" with respect to the number of amino acids encompassed within the epitope recognized by the claimed digital antibodies in claim 1. The correct test for anticipation is whether Belov et al. teach at least 15 antibodies each recognizing an epitope consisting of 3 amino acids or 4 amino acids, which is what is claimed. Belov et al. do not teach or suggest at least 15 antibodies that each recognize an epitope consisting of 3 or 4 amino acids. Belov et al. teach a microarray comprised of antibodies that each specifically binds to a particular cell surface antigen. As discussed in the telephone interview, if the microarray taught by Belov et al. contained antibodies that bind epitopes of 3 or 4 amino acids each recognizing a plurality of proteins, as currently claimed, this array would not be useful for the purpose for which it is designed, *i.e.*, determination of presence or absence of a cell surface protein by detection of binding of a single antibody on the array to a single protein of interest. Cross-reactivity of the antibodies in the array of Belov et al. towards multiple proteins would not provide useful information in the context of the purpose for which the array was designed. Therefore, a set of at least 15 antibodies which each binds an epitope consisting of 3 or 4 amino acids, wherein each antibody recognizes a plurality of proteins that comprise the epitope to which the antibody binds, is not inherently disclosed in Belov et al.

The Examiner cites Northrup et al. (U.S. Patent No. 6,410,245), col. 15, lines 45-50, as disclosing that epitopes recognized by antibodies can be at least about 3 consecutive amino acids long. Applicants respectfully note that Northrup et al. merely state that a cell surface reporter may comprise "at least one segment (*e.g.*, an epitope of at least about 3 consecutive amino acids) that is not present in a naturally-occurring cell surface protein." This reference does not state that the stretch of 3 amino acids that does not naturally occur in the cell surface protein is the *only* epitope recognized by an antibody, as in the present claims which recite that the epitope "consists of" 3 or 4 amino acids. The 3 amino acids referred to in Northrup et al. may be part of a larger epitope

recognized by an antibody. In any case, Northrup et al. do not disclose any digital antibodies, much less a set of at least 15 digital antibodies as claimed in the present application. As disclosed in the specification, antibodies that bind small linear peptide epitopes have been previously described (paragraph [0092] and Table 2). However, the claims of the present application are directed to *a set of at least 15 digital antibodies*. Neither of the cited references, Belov et al. or Northrup et al., teach such a set of antibodies that recognize epitopes consisting of 3 or 4 amino acids.

The Examiner states that Applicants' arguments that the present invention is distinguishable over Belov et al. on the basis that the claimed digital antibodies are cross-reactive are not persuasive because "[t]he distinguishing features outlined by applicant are not recited in the claim language." Office Action, page 5, emphasis in original. Applicants respectfully disagree with this statement. The specification states that "[b]y virtue of the epitope specificity, digital antibodies generally recognize a multiplicity of proteins that comprise the small epitope to which the antibody binds." Paragraph [0082]. The specification also states that "a single digital antibody generally binds a plurality of proteins . . . based on the presence of the cognate small epitope within the plurality of bound proteins." Paragraph [0054]. Thus, the distinguishing features to which the Examiner refers are implicitly recited in the claims by virtue of recitation of the term "digital antibody." However, the claims have been amended herein to recite that "each digital antibody recognizes a plurality of proteins that comprise the small epitope to which the antibody binds," solely for purposes of clarification and without acquiescing to any of the rejections.

In view of the foregoing, Applicants respectfully request reconsideration and withdrawal of the rejection under 35 U.S.C. §102(b).

***Rejection under 35 U.S.C. § 102(e)***

Claims 1-30 are rejected under 35 U.S.C. §102(e) as allegedly unpatentable over Chait et el. (U.S. Patent Application 2003/0045694). Applicants respectfully traverse this rejection for reasons of record in the response filed on September 28, 2004, and for reasons discussed hereinbelow.

Chait et al. do not teach a set of digital antibodies that each bind a different epitope consisting of 3 or 4 consecutive amino acids, wherein each antibody in the set recognizes a plurality of proteins comprising the epitope to which the antibody binds, as currently claimed. Since Chait et al. do not teach antibodies that bind epitopes consisting of 3 or 4 amino acids or antibodies each recognizing a plurality of proteins comprising the epitope to which the antibody binds, Chait et al. do not anticipate the claimed invention.

Chait et al. teach a microarray comprised of antibodies that each specifically binds to a particular protein to which a DNA tag has been attached as part of a detection methodology. As discussed in the telephone interview, if the microarray taught by Chait et al. contained antibodies that bind epitopes of 3 or 4 amino acids each recognizing a plurality of proteins, as currently claimed, this array would not be useful for the purpose for which it is designed, *i.e.*, detection of protein molecules by binding of a single antibody on the array to a single protein of interest. Cross-reactivity of the antibodies in the array of Chait et al. towards multiple proteins would not provide useful information in the context of the purpose for which the array was designed. Therefore, a set of at least 15 antibodies which each binds an epitope consisting of 3 or 4 amino acids, wherein each antibody recognizes a plurality of proteins that comprise the epitope to which the antibody binds, is not inherently disclosed in Chait et al.

The Examiner states that Applicants' arguments that the present invention is distinguishable over Chait et al. on the basis that the claimed digital antibodies are cross-reactive are not persuasive because the claims do not recite this feature. Office Action, page 6. Applicants respectfully disagree with this statement, and maintain that this feature is implicitly recited in the claims by virtue of recitation of the term "digital antibody," as discussed above. However, the claims have been amended herein to recite that "each digital antibody recognizes a plurality of proteins that comprise the small epitope to which the antibody binds," solely for purposes of clarification and without acquiescing to any of the rejections.

In view of the foregoing, Applicants respectfully request reconsideration and withdrawal of the rejection under 35 U.S.C. §102(e).

***Rejection under 35 U.S.C. § 103(a)***

Claims 2-8 stand rejected under 35 U.S.C. § 103(a) as allegedly unpatentable over Belov et al. as in view of Chait et al.[1] Applicants respectfully traverse this rejection for reasons of record in the response filed on September 28, 2004, and for reasons discussed hereinbelow.

As discussed above, neither Belov et al. nor Chait et al., teaches a set of at least 15 digital antibodies each binding an epitope consisting of 3 or 4 amino acids, wherein each digital antibody recognizes a plurality of proteins that comprise the small epitope to which the antibody binds. The combination of these references also does not teach or suggest a set of digital antibodies with these claimed features. Since the combination of the references does not teach or suggest all of the claim limitations, a *prima facie* case of obviousness has not been established. MPEP §2142.

In view of the foregoing, Applicants respectfully request reconsideration and withdrawal of the rejection under 35 U.S.C. §103(a).

***Withdrawal of previous rejection under 35 U.S.C. §112, second paragraph***

Applicants acknowledge with appreciation the withdrawal of the previous rejection under 35 U.S.C. §112, second paragraph, to the extent that it has not been reiterated in this Office Action. Applicants would appreciate the Office officially withdrawing this rejection.

[1] The text of the rejection on page 4 of the Office Action refers to "Cardone et al." However, since the Examiner has not provided a citation for "Cardone et al.," Applicants assume that the Examiner meant to refer to Chait et al. The response to this rejection has been drafted accordingly.

## CONCLUSION

In view of the above, each of the presently pending claims in this application is believed to be in immediate condition for allowance. Accordingly, the Examiner is respectfully requested to withdraw the outstanding rejection of the claims and to pass this application to issue. If it is determined that a telephone conference would expedite the prosecution of this application, the Examiner is invited to telephone the undersigned at the number given below.

In the event the U.S. Patent and Trademark office determines that an extension and/or other relief is required, Applicants petition for any required relief including extensions of time and authorize the Commissioner to charge the cost of such petitions and/or other fees due in connection with the filing of this document to Deposit Account No. 03-1952 referencing docket no. 559312000100. However, the Commissioner is not authorized to charge the cost of the issue fee to the Deposit Account.

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